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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,889	09/10/2007	Ralph Biemans	VB60395	4156

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GLAXOSMITHKLINE
CORPORATE INTELLECTUAL PROPERTY, MAI B482
FIVE MOORE DR., PO BOX 13398
RESEARCH TRIANGLE PARK, NC 27709-3398

EXAMINER	
GANGLE, BRIAN J	
ART UNIT	**PAPER NUMBER**
1645	

NOTIFICATION DATE	DELIVERY MODE
09/23/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USCIPRTP@GSK.COM
LAURA.M.MCCULLEN@GSK.COM
JULIE.D.MCFALLS@GSK.COM

Office Action Summary	Application No.	Applicant(s)	
	10/525,889	BIEMANS ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23 and 35-50* is/are pending in the application.

4a) Of the above claim(s) *43,44 and 47-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23, 35-42, and 45-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/25/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 8/6/2009 is acknowledged. Claim 23 is amended. Claims 1-22 and 24-34 are cancelled. New claims 35-50 are added.

Election/Restrictions

Applicant's election of Group III in the reply filed on 8/6/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant asserts that new claims 35-50 are dependent on claim 23 and are thus directed to the elected invention. To the contrary, claims 35-42 and 45-46 are directed to the elected invention. Claims 43-44 and 47-50 are directed to nonelected Group II. While these claims are dependent on claim 23 in the sense that they refer to claim 23, they are not dependent on claim 23 in that they do not require all of the limitations of claim 23. In fact, these claims are in essence no different than the previous claims of Group II. The purification or production of a product by a particular process (i.e. the instant recombinant) does not impart novelty or unobviousness to a product when the product is taught by the prior art. This is particularly true, when the properties of the product are not changed by the process in an unexpected manner. *In re Thorpe*, 227 USPQ 964 (CAFC 1985); *In re Marosi*, 218 USPQ 289, 292-293 (CAFC 1983); and *In re Brown*, 173 USPQ 685 (CCPA 1972). Therefore, even if a particular process used to prepare a product is novel and unobvious over the prior art, the product *per se*, even when limited to the particular process, is unpatentable over the same product taught by the prior art. *In re King*, 107 F.2d 618, 620, 43 USPQ 400, 402 (CCPA 1939); *In re Merz*, 97 F.2d 559, 601, 38 USPQ 143-45 (CCPA 1938); and *United States v. Ciba-Geigy Corp.*, 508 F.supp. 1157, 1171, 211 USPQ 529, 543 (DNJ 1979).

Claims 43-44 and 47-50 are withdrawn as being drawn to nonelected inventions. Claims 23, 35-42, and 45-46 are currently under examination.

Information Disclosure Statement

The information disclosure statement filed on 2/25/2005 has been considered. References AE-AH were not considered because they are duplicates of references AA-AD. The other references that have been lined through were not considered because no copy of the reference has been provided. Applicant has stated that the references on the IDS were cited on the International Search Report and that applicant understands that copies were supplied by the International Bureau. This is not the case. No copies of any of the references have been provided. The references that have been considered are references for which the examiner has provided a copy and cited on a PTO-892 form.

Specification

This application fails to comply with the requirements of 37 C.F.R. 1.821-1.825 because it contains amino acid and/or nucleotide sequences that are not identified. For example, figures 2-3 and pages 38, 40, and 50 contain sequences that are not identified. Appropriate sequence identifiers should be used to comply with sequence rules. The sequences in the specification should match the sequence listing and computer readable form (CRF) submitted with the application. Applicant is asked to review the specification for sequences that are not identified and correction is required. Applicant must provide a substitute computer readable form (CRF) copy of the "Sequence Listing", a substitute paper copy of the "Sequence Listing", an amendment of the specification to insert appropriate sequence identifiers, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

The use of the trademarks BRIJ, TRITON, and TWEEN have been noted in this application on pages 12, 13, and 27. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

It is noted that the cited occurrences of improper use are only exemplary and applicant should review the specification to correct any other use of trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23, 35-42, and 45-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 is rendered vague and indefinite by step (e), which recites "contacting a solubilized NspA protein with a refolding buffer." Step (d) recites "optionally solubilizing at least part of the inclusion body and the NspA protein." Since step (e) requires an NspA protein that has been solubilized, step (d) cannot be optional.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 45, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Brodeur *et al.* (WO 96/29412, 1996).

The instant claims are drawn to a method of preparing a medicament containing an isolated, refolded NspA protein comprising the steps of contacting a solubilized NspA protein with a refolding buffer. The method includes optional steps of expressing NspA in a host cell, breaking the host cell to obtain an inclusion body comprising the NspA protein, washing the inclusion body, solubilizing the protein, and removing the refolding buffer from the NspA protein.

Brodeur *et al.* disclose preparation of compositions comprising folded NspA from *Neisseria meningitidis* and *Neisseria gonorrhoeae* (see page 13, lines 20-34). As disclosed in the

instant specification on page 17, the protein disclosed by Brodeur *et al.* is NspA and as disclosed in Figure 1 and on page 51, the folded NspA migrates on SDS-PAGE gels at 22 kDa, as opposed to the denatured protein which migrates at 18 kDa. The NspA disclosed by Brodeur *et al.* migrates at 22 kDa; therefore, it is the folded version, and where Brodeur *et al.* disclose contacting the protein with Zwittergent 3, 14 (see page 64), the Zwittergent 3,14 serves as a refolding buffer.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23, 35-42, and 45-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jansen *et al.* (Biochim Biophys Acta, 1464:284-298, 2000) in view of Brodeur *et al.* (WO 96/29412, 1996).

The instant claims are drawn to a method of preparing a medicament containing an isolated, refolded NspA protein comprising the steps of contacting a solubilized NspA protein with a refolding buffer. The method includes optional steps of expressing NspA in a host cell, breaking the host cell to obtain an inclusion body comprising the NspA protein, washing the inclusion body, solubilizing the protein, and removing the refolding buffer from the NspA protein.

Jansen *et al.* teach a method of producing a composition comprising isolated, refolded PorA from *Neisseria meningitidis* from inclusion bodies expressed in *E. coli* (see page 285, column 2, paragraphs 1-2). In the method, transformed *E. coli* cells were sonicated and inclusion bodies were collected by centrifugation, then solubilized in urea (paragraph bridging pages 285-286). The proteins in the inclusion body were then contacted with a buffer containing SB-12 at 0.5% and ethanolamine at 20 mM, pH 10.8 (see page 286, column 1, paragraphs 2-3 and page 289, column 1). Jansen *et al.* state that the SB-12 was purified according to the method of

Dekker *et al.* (Eur. J. Biochem., 232:214-219, 1995), who purified the sB-12 by passing it over an Al_2O_3 column.

The disclosure of Jansen *et al.* differs from the instant invention in that they folded PorA instead of NspA, they disclose an SB-12 concentration of 0.5% instead of 0.2%, and the pH of the buffer is 10.8 instead of 11.

Brodeur *et al.* disclose preparation of compositions comprising folded NspA from *Neisseria meningitidis* and *Neisseria gonorrhoeae* (see page 13, lines 20-34). As disclosed in the instant specification on page 17, the protein disclosed by Brodeur *et al.* is NspA. Brodeur *et al.* further disclose that NspA is a highly conserved, unique antigen that provides the basis for new immunotherapeutic, prophylactic, and diagnostic agents useful in the treatment, prevention and diagnosis of *Neisseria meningitidis* diseases (see page 1, lines 6-11). As disclosed in the instant specification on page 17, the protein disclosed by Brodeur *et al.* is NspA and as disclosed in Figure 1 and on page 51, the folded NspA migrates on SDS-PAGE gels at 22 kDa, as opposed to the denatured protein which migrates at 18 kDa. The NspA disclosed by Brodeur *et al.* migrates at 22 kDa; therefore, it is the folded version, and where Brodeur *et al.* disclose contacting the protein with Zwittergent 3, 14 (see page 64), the Zwittergent 3,14 serves as a refolding buffer.

It would have been obvious to one of ordinary skill in the art, at the time of invention, to substitute neisserial NspA for neisserial PorA in the folding method of Jansen because NspA is a highly conserved, unique antigen that provides the basis for new immunotherapeutic, prophylactic, and diagnostic agents useful in the treatment, prevention and diagnosis of *Neisseria meningitidis* diseases and the protein should be in native, folded form to preserve its native antigenicity. With regard to the concentration of SB-12 and the pH of the buffer, generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid

concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). In this case, the specification describes the use of SB-12 in concentrations of at least about 0.2% and states that "preferably" the pH is about 11.0. Therefore, there is no evidence that the specifically claimed concentration and pH are critical to the invention.

One would have had a reasonable expectation of success because NspA is folded buffer containing Zwittergent 3, 14, which is very similar to SB-12 (also known as Zwittergent 3,12). In addition, as evidenced by the instant specification, one would have had a reasonable expectation of success in altering the pH and SB-12 concentration.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian J Gangle/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645